We additionally recommend that each Drug Watch listing include a link to a description of potential data sources, ranked from most to least valid, with adequate explanation of their potential shortcomings. This will help to add transparency to the process and may assist healthcare practitioners in understanding the nature of the emerging safety issue.

Quality Control

FDA should monitor and evaluate the accuracy of postings with respect to the number and percent of "false positives" – those postings for which drug-injury causation was not found. These evaluations will inform FDA how to improve data selection, weighting and analyses.

Communications

Background

In response to calls for earlier warnings of possible drug safety issues, "FDA has concluded it should do more to make drug information available as it emerges while the Agency is evaluating its significance" (lines 59-60). This is clearly a double-edged sword: communicating unsubstantiated reports of possible drug safety issues to the public has the potential to do harm as well as good. The analytical complexities of identifying emerging safety issues are discussed in detail above. A benefit of earlier reporting may be realized when the reports presage accurately a real causal relationship. Getting patients to talk with a doctor earlier about whether a medicine is appropriate for them, given a reassessment of the benefit-risk balance in light of the new information, could save pain, suffering and lives. The downside of reporting unsubstantiated data happens when two conditions occur at the same time: when the reports are false positives (when they do not represent a real drug-injury relationship) and when people have, on the basis of the reports, stopped taking a needed medicine, incurring unnecessary pain, suffering, and in some cases, premature death. As in all activities, Drug Watch must balance potential benefits with potential risks, alerting doctors and patients appropriately while avoiding frightening patients and confusing doctors' practice of medicine. Accurate, appropriate and effective communication is essential to the success of Drug Watch. The following remarks address Drug Watch communications topics pertinent to the major stakeholders: patients, doctors, sponsors and the FDA.

Communicating Risks

There has been much research in the past 40 years about how persons evaluate risks, leading to a growing body of empirical evidence about the use of cognitive skills in assessing risk, the use of heuristics (i.e., mental shortcuts) when risk concepts tax those skills, the biases those heuristics have on risk perceptions, and our abilities to understand risk concepts and communications. There is still much uncertainty, however, about how individuals personally characterize risks, how best to communicate risks to the public, and whether and how persons understand risk concepts and communication. We strongly recommend that, given the importance of risk communications in Drug Watch and the risks of giving confusing and possibly harmful information to the public, FDA seek the advice and counsel of experts in risk communication, researchers in cognitive psychology and practicing physicians about how to report emerging risks on the public web site.

Recent models of cognition[1] propose that persons rely on two distinct cognitive skills in making decisions: reasoning and intuition. Reasoning is slow, deliberate and effortful; intuition is fast and effortless. Persons typically rely on their intuition when making decisions, monitoring those decisions with reasoning. However, since cognitive capacity

[1] Kahneman, Daniel, Maps of Bounded Rationality: Psychology for Behavioral Economic, The American Economic Review, Vol. 93, No. 5, December 2003.

is limited by elements such as time pressures, amount of information or complexity of information, we are often lax in our reasoning, resulting in errors in judgment. Given low health literacy rates and general innumeracy of a large proportion of the population, risk concepts are particularly difficult to understand, even more so under time pressures and complexity typically present in medical care situations. Under such circumstances, many people use mental shortcuts to try to understand difficult risk concepts, relying on a wide range of heuristics that color or bias perceptions of risk.[2,3,4,5,6] Perceptions of risk also are affected, and can be manipulated, by how the risks are presented, including how concepts are framed and whether context is provided. Since persons responsible for communicating risks have the ability to manipulate perceptions and behavior, those persons must examine closely the ethical implications of their risk-information program. The Drug Watch initiative places FDA squarely in the position of potentially scaring persons away from taking needed medicines: "Merely mentioning possible adverse consequences (no matter how rare) of some product or activity could enhance their perceived likelihood and make them appear more frightening."[7]

Innumeracy among the public makes communication of risk especially difficult, so alternatives to written documentation such as graphics and other visual representations to enhance the public's understanding of risk have been proposed.[8] Unfortunately, there is still much uncertainty as to the impact of visuals on comprehension, and the future research agenda in this area remains robust.[9] One recent study of the impact of visuals on comprehension and motivation suggests that the actual use of information increases when cognitive effort is reduced, when the decision-maker is moved closer to the actual experience, and when the meaning of information is highlighted for the decision-maker.[10] This research also highlights the importance of experience, skill and motivation of users, suggesting the need for an array of information-presentation formats to optimize comprehension by users. Very recent research has reaffirmed the role of the heuristic of "affect," or feeling (like-dislike, approach-avoid, etc.), at the core of decision-making, suggesting that an appeal to affect in information-presentation formats may be very

---

[2] Covello, Vincent T., Detlof von Winterfeldt and Paul Slovic, Risk Communication: A Review of the Literature, Risk Abstracts, 3, 171-182. October 1986.
[3] Fischoff, Baruch, Ann Bostrom and Marilyn Jacobs Quadrel, Risk Perception and Communication, in Detels, R., McEwen, J., Beaglehole, R. & Tanaka, H., Oxford Textbook of Public Health, 4th ed. Oxford University Press, 2002.
[4] Slovic, Paul, The Perception of Risk, Earthscan Publications Ltd., 2000
[5] Heuristics and Biases, The Psychology of Intuitive Judgment, Gilovich, Thomas, Dale Griffin and Daniel Kahneman, eds. Cambridge University Press, 2002.
[6] Slovic, Paul, Ellen Peters, Gretchen Dieck, Susan Berger and John Grana, Risk Perception of Prescription Drugs, Results of a National Survey; (in review, Risk Analysis)
[7] Slovic, Paul, Informing and Educating the Public About Risk, Risk Analysis, Vol. 6, No. 4, 1986.
[8] Peters, Ellen, Daniel Vastfjall, Paul Slovic, C.K. Mertz, Ketti Mazzocco and Stephan Dickert, Numeracy and Decision Making, in press, Psychological Science.
[9] Lipkus, Isaac M., J. G. Hollands, The Visual Communication of Risk, Journal of the National Cancer Institute Monographs No. 25, 1999.
[10] Hibbard, Judith H. and Ellen Peters, Supporting Informed Consumer Health Care Decisions: Data Presentation Approaches that Facilitate the Use of Information in Choice, Annual review of Public Health, 2003, 24:413-33.

helpful in therapeutic contexts.[11] The ethical implications of the manipulations of affect are obvious. Recent dramatic progress of biomedical science has increased both the quantity and quality of new drugs, making the communication of their risks and benefits even more challenging and critical, drawing the focus of the Agency for Healthcare Research and Quality.[12] Potential solutions have been outlined, including enhanced education of health care providers, increased motivation of patients and families, use of creative communication technologies, and better organization of and access to medical records and information.

This brief overview of risk evaluation and communication research is not meant to be exhaustive; rather, it is a cautionary statement of the complexity and criticality of conveying unsubstantiated, emerging safety data to the public. We reiterate our recommendation for FDA to consult with experts in the field of risk communication, cognitive psychologists and practicing physicians before launching this aggressive program, in order to avoid the potential untoward impacts of confusing or faulty communication.

Communicating the Benefit-Risk Balance

FDA states that it is making information on emerging safety issues available "... so that patients and healthcare professionals will have the most current information concerning the potential risks and benefits of a marketed drug ..." (lines 66-67). We heartily agree with the sentiment that the benefits as well as risks of a drug should be included on each listing of Drug Watch; unfortunately, the guidance does not address this issue.

In the questions and answers addendum to the guidance, FDA states the following: "FDA makes decisions about the safety of a particular drug after considering its benefit to treat a particular condition in relation to its risks. FDA therefore considers a drug safe when its benefits outweigh its risks for its intended use" (question 7). As this statement indicates, drug safety is not defined by a medicine's potential or real risks, but rather by the balance of risks and benefits characterizing it. Another critical consideration in drug safety is the acknowledgement that all drugs pose risks, as does the choice not to take a needed medicine. Consequently, physicians and consumers must focus *not* on the absolute risk of the drug, but on its benefit-risk balance and to the underlying disease, if left untreated. Communication of these fundamental truths about drug safety is crucial, and they should be an overarching theme of Drug Watch. Each and every communication to the public through Drug Watch should contain this balance of risk and benefit information, reminding what the drug is used for in the first place as well as what may be its potential or emerging risks. Drug Watch must be designed to report on safety, not risk. Otherwise, with a sole focus on risks, patients may be unnecessarily frightened

---

[11] E. Peters, (in press) "The functions of affect in the construction of preferences," in S. Lichtenstein & P. Slovic (Eds.), The Construction of Preference, Cambridge University Press.
[12] Campbell, William H. and Robert M. Califf, Improving communication of drug risks to prevent patient injury: proceedings of a workshop, Pharmacoepidemiology and Drug Safety 2003; 12: 183-194.

from taking needed medicines, the physician-patient relationship will be interfered with, and Drug Watch will not promote the safe use of medicines.

It is also critical to keep in mind that because of unique biological makeup and specific environmental circumstances, individuals will respond differently to a given drug. As a result, a medicine's benefit-risk balance and relative risk will be different for individual patients. Presenting both benefit and risk information will enable physicians and patients to make a balanced decision that is best for an individual patient. Drug Watch should also provide contextual information that will enable physicians to decipher how the emerging safety information likely impacts the benefit-risk balance for a specific patient.

Communicating Results of Evaluation of Emerging Information

FDA also must consider what information would be provided once it has completed its analysis of an emerging safety risk. In instances where it is concluded that there is no link between emerging risk information and a specific drug, FDA must ensure that this finding is communicated clearly and quickly so that physicians do not alter their prescribing practices needlessly, potentially putting their patients at great risk. FDA must also determine whether to remove the drug from the Drug Watch.

For the public health, communicating removal of a drug from the Drug Watch list can be as important as posting one, since persons who have stopped taking a needed drug after it is listed on Drug Watch may be suffering needlessly or are at higher risk of experiencing the consequences of their underlying disease. Trying to discredit claims after making them familiar to older adults also may sometimes backfire, increasing their tendency to call those claims true.[13] We recommend, where appropriate, that FDA make it absolutely clear on the Drug Watch web site that, after further analysis, there is no safety problem and the drug is safe, or that the drug was not found to be unsafe. Also, where appropriate, FDA should make it clear that the issue has been resolved and a change has been made to prescribing instructions (the label), and that these new instructions should be discussed with the prescribing physician. These messages should be highlighted on the Drug Watch central page, with attention-focusing graphics that announce "New Information About Drug X." And, of course, patient and physician information sheets should be revised immediately.

We recommend that information on the removal of a drug from Drug Watch should remain on the public web site for a length of time sufficient to assuage public fears, perhaps a year. A link should be included that describes all decisions about a drug that is posted on Drug Watch. This is important for liability concerns, too, to prevent the unnecessary medical costs of spurious litigation.

---

[13] Skurnik, Ian, Carolyn Yoon, Denise C. Park and Norbert Schwarz, How Warnings About False Claims Become Recommendations, Journal of Consumer Research, March 2005.

Avoiding Unintended Consequences

The Drug Watch website has the potential to dramatically alter FDA's drug safety communication to physicians and patients. To ensure that Drug Watch is used as a tool to benefit, rather than hurt, public health, however, FDA must promote judicious and appropriate use of the website information. To this end, FDA should be thoughtful and cautious in disseminating emerging safety information, and it should partner with physicians, patients, drug sponsors and the general public to ensure that Drug Watch is used to benefit patients and advance our knowledge of medicines.

Overreaction to Drug Risks

Several unintended consequences could undermine the effectiveness of Drug Watch and potentially threaten patient health. For example, physicians may overreact to the emerging risk information on Drug Watch and become overly-cautions in prescribing drugs listed on Drug Watch. Similarly, some physicians might opt to discontinue all of their patients from a drug posted on Drug Watch. Excessive caution could result from a number of factors including physicians' lack of understanding of the preliminary nature of the safety information on Drug Watch or a conscious decision to practice "defensive medicine" to minimize potential malpractice suits. Physician overreaction could have major deleterious consequences for patients if they are needlessly switched to alternative medications, which may be less effective or have more serious side effects for them, or if the physician discontinues treatment because no other alternative to the drug exists. In such instances, a patient may be denied access to appropriate medical care.

Undermining of the Physician-Patient Relationship

Another unintended consequence could be an undermining of trust in physicians if they are not armed with sufficient information to answer patients' questions on potential safety concerns posted on Drug Watch. Alternatively, physicians' credibility may be questioned if they are unable to communicate effectively to their patients why they should continue treatment with a medicine listed on Drug Watch. Both situations could harm the doctor-patient relationship. These situations may also lead to patients deciding unilaterally to discontinue a needed treatment despite the advice of their physician. The consequences of such a decision could be dire since discontinuing a needed medicine may pose a much greater risk to the health of the patient than would exposure to a drug's potential side effects.

Increased Liability for Physicians

Another inadvertent effect could be increased liability for the physician arising from a new responsibility to monitor and be conversant in the most current information posted on Drug Watch. Given the increasing demands on their time due to managed care pressures and rapid pace of medical advances, physicians likely will find it exceedingly challenging to keep abreast of the latest postings on Drug Watch and to translate how the

information is relevant for individual patients. The ambiguity of the information on Drug Watch likely will expose physicians to increased liability, even in instances where no causal link can be established between a drug and an adverse event. FDA should consider how it might dissuade third parties from misusing Drug Watch to file frivolous lawsuits.

Inhibition of Clinical Trial Enrollment

A fourth inadvertent effect may be the impact of Drug Watch on clinical trial enrollment: Risk information posted on a website could have a negative impact on ongoing clinical trials as it may cause unnecessary concern to clinical investigators and patients. Specifically, it may prejudice physicians against recommending their patients for a clinical trial of a drug listed on Drug Watch or it may cause trial participants to withdraw their consent despite the counsel of their physician or the clinical trial investigator. Also, clinical investigators might be discouraged from participating in clinical trials because of liability or other concerns. This would be an unfortunate consequence given the preliminary nature of the information posted on Drug Watch, coupled with the challenges clinical trial sponsors face in identifying appropriate enrollees for the trials. Highlighting emerging risks also may cause physicians and patients to overemphasize all drugs' risks relative to their benefits, and thus deter persons from involvement in clinical trials of any drug. Further confusion to patients and investigators could ensue if drug sponsors are required to update investigator brochures each and every instance of a change in status of a drug on Drug Watch. Any activity that would discourage clinical trial enrollment based on unwarranted safety concerns would do a great disservice to the continued development of new life-saving medicines.

Communication to Patients and Consumers

Clarity of Language

FDA states "... listing of a drug on the Drug Watch should not be construed as a statement by the FDA that the drug is dangerous ..." (lines 24-25). We concur, but ask what steps can be taken to ensure that such interpretation does not occur. We recommend that FDA make a clear and bolded statement on each Drug Watch posting using exactly that statement about not misconstruing a listing, with an additional statement that persons using the posted drug should not rush to judgment and discontinue their medication without discussing the use of the drug with their doctor.

FDA states: "Our goal with the Drug Watch is to share emerging safety information before we have fully determined its significance or taken final regulatory action so that patients and healthcare professionals will have the most current information concerning the potential risks and benefits of a marketed drug product upon which to make individual treatment decisions" (lines 64-68). If FDA is still analyzing information while posting it, not yet having reached a conclusion about a drug's safety, we do not think it realistic to expect that patients or even healthcare providers will be able to make proper sense of the situation either. This situation is particularly acute for most patients who are